10/629,975 Wodaked Search WCook 6/7/05

dhis

(FILE 'HOME' ENTERED AT 12:08:06 ON 07 JUN 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 12:08:27 ON 07 JUN 2005

L1	1	S	LACTOFERRIN?	AND	450NM	
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297 S LACTOFERRIN AND POLYCLONAL?

L3 36 S L2 AND ENDOGENOUS?

1 S L3 AND FECAL?

L5 13 S L3 AND ENZYME?

L6 13 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=>

L2

L4

d his

(FILE 'HOME' ENTERED AT 12:08:06 ON 07 JUN 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 12:08:27 ON 07 JUN 2005

L1 1 S LACTOFERRIN? AND 450NM

297 S LACTOFERRIN AND POLYCLONAL?

L3 36 S L2 AND ENDOGENOUS?

1 S L3 AND FECAL?

L5 13 S L3 AND ENZYME?

L6 13 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=>

L2

L4

ANSWER 6 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN 96252064 EMBASE ΑN 1996252064 DN Anti-lactoferrin autoantibodies: Relation between epitopes and ΤI iron-binding domain. Audrain M.A.P.; Gourbil A.; Muller J.-Y.; Esnault V.L.M. AU Laboratoire d'Immunologie, CHU, 9 quai Moncousu,44035 Nantes Cedex, France CS Journal of Autoimmunity, (1996) Vol. 9, No. 4, pp. 569-574. SO ISSN: 0896-8411 CODEN: JOAUEP CY United Kingdom Journal; Article DTFS General Pathology and Pathological Anatomy 005 Cardiovascular Diseases and Cardiovascular Surgery 018 026 Immunology, Serology and Transplantation LΑ English SLEnglish Entered STN: 960924 ED Last Updated on STN: 960924 Anti-neutrophil cytoplasm antibodies (ANCA) have been found in the sera of ΔR patients presenting systemic necrotizing microscopic vasculitis, i.e. Wegener's granulomatosis and microscopic polyangiitis. Lactoferrin (LF) is one of the antigens rarely recognized by ANCA, and anti-LF autoantibodies are found in several autoimmune conditions, including rheumatoid vasculitis, rheumatoid arthritis, systemic lupus erythematosus, ulcerative colitis, primary sclerosing cholangitis and Crohn's disease. We analysed the epitopes recognized by human anti-LF antibodies to test whether the heterogeneity of clinical presentation might be due to a different epitope recognition profile. Several monoclonal antibodies were raised and used in competition studies with six human sera. Four distinct epitopes were identified on LF, and LF binding of only one of six sera was inhibited by one of the monoclonals. Thus, anti-LF autoreactivity appears to be polyclonal and not restricted to an immunodominant epitope. Specific epitope profiles cannot be determined in these autoimmune conditions. We hypothesized that the interaction of anti-LF antibodies with the LF iron binding domain might contribute to pathogenesis by inhibiting iron chelation after neutrophil activation, thereby providing increased iron availability for endothelial cell damage. The relation of anti-LF mouse monoclonals or polyclonal human or rabbit antibodies to the LF iron-binding domain was studied in competition assays between 59Fe and these antibodies. Preincubation of LF with monoclonals or anti-LF human sera did not affect the binding of 59Fe on LF. 59Fe-binding kinetic studies showed that rabbit anti-LF polyclonal, but not mouse monoclonals or human anti-LF positive sera, was capable of inhibiting iron binding on Therefore, anti-LF autoantibodies did not appear to modulate LF iron-binding activity. We conclude that LF is a rare antigen specificity for ANCA and that the clinical and pathophysiological relevance of anti-LF autoreactivity remains uncertain. CTMedical Descriptors: \*autoimmunity \*iron binding capacity \*systemic vasculitis: DI, diagnosis \*systemic vasculitis: ET, etiology controlled study enzyme linked immunosorbent assay human kinetics major clinical study priority journal

diagnosis etiology

Drug Descriptors:

\*autoantibody: EC, endogenous compound \*epitope

\*granulocyte antibody: EC, endogenous compound
\*lactoferrin: EC, endogenous compound
monoclonal antibody
(lactoferrin) 55599-62-7

RN

```
ANSWER 3 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
     1999070895 EMBASE
AN
     Measurement of urinary lactoferrin as a marker of urinary tract
TI
     infection.
     Arao S.; Matsuura S.; Nonomura M.; Miki K.; Kabasawa K.; Nakanishi H.
CS
     S. Matsuura, Research and Development Department, Iatron Laboratories,
     Inc., 1460-6, Mitodai Mito, Tako, Katori, Chiba 289-2247, Japan
     Journal of Clinical Microbiology, (1999) Vol. 37, No. 3, pp. 553-557.
SO
     Refs: 27
     ISSN: 0095-1137 CODEN: JCMIDW
     United States
CY
     Journal; Article
DT
FS
             Microbiology
     004
     028
             Urology and Nephrology
LΑ
     English
\operatorname{SL}
     English
ED
     Entered STN: 19990311
     Last Updated on STN: 19990311
AB
     The usefulness of the measurement of urinary lactoferrin (LF)
     released from polymorphonuclear leukocytes and of an immunochromatography
     test strip devised for measuring urinary LF for the simple and rapid
     diagnosis of urinary tract infections (UTI) was evaluated. Urine
     specimens were collected from apparently healthy persons and patients
     diagnosed as suffering from UTI. In the preliminary study, the LF
     concentrations in 121 normal specimens and 88 specimens from patients (60
     with UTI) were quantified by an enzyme-linked immunosorbent
            The LF concentration was 3,300.0 \pm 646.3 ng/ml (average \pm
     standard error of the mean) in the specimens from UTI patients, whereas it
     was 30.4 \pm 2.7 ng/ml and 60.3 \pm 14.9 ng/ml in the specimens from
     healthy persons and the patients without UTI, respectively. Based on
     these results, a 200-ng/ml LF concentration was chosen as the cutoff value
     for negativity. Each urine specimen was reexamined with the newly devised
     immunochromatography (IC) test strip to calculate the indices of efficacy.
     Based on the cutoff value, it was calculated that the sensitivity,
     specificity, and positive and negative predictive values of the IC test
     were 93.3, 89.3, 86.2, and 94.9%, respectively, compared with the results
     of the microscopic examination of the urine specimens for the presence of
     leukocytes. The respective indices for UTI were calculated as 95.0, 92.9,
     89.7, and 96.6%. The tests were completed within 10 min. These results
     indicated that urine LF measurement with the IC test strip provides a
     useful tool for the simple and rapid diagnosis of UTI.
СТ
     Medical Descriptors:
     *urinalysis
     *disease marker
     *urinary tract infection: DI, diagnosis
     measurement
     chromatography
       enzyme linked immunosorbent assay
     diagnostic accuracy
     microscopy
     intermethod comparison
     neutrophil
    human
    male
     female
     major clinical study
     controlled study
    human cell
    adolescent
     aged
     child
```

adult

article
priority journal
Drug Descriptors:
 \*lactoferrin: EC, endogenous compound
 polyclonal antibody
monoclonal antibody
RN (lactoferrin) 55599-62-7

```
ANSWER 3 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
     1999070895 EMBASE
AN
     Measurement of urinary lactoferrin as a marker of urinary tract
ΤI
     infection.
     Arao S.; Matsuura S.; Nonomura M.; Miki K.; Kabasawa K.; Nakanishi H.
ΑU
     S. Matsuura, Research and Development Department, Iatron Laboratories,
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     Inc., 1460-6, Mitodai Mito, Tako, Katori, Chiba 289-2247, Japan
     Journal of Clinical Microbiology, (1999) Vol. 37, No. 3, pp. 553-557.
SO
     Refs: 27
     ISSN: 0095-1137 CODEN: JCMIDW
     United States
CY
DT
     Journal; Article
             Microbiology
FS
             Urology and Nephrology
LА
     English
SL
     English
     Entered STN: 19990311
ED
     Last Updated on STN: 19990311
AB
     The usefulness of the measurement of urinary lactoferrin (LF)
     released from polymorphonuclear leukocytes and of an immunochromatography
     test strip devised for measuring urinary LF for the simple and rapid
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     *urinalysis
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     measurement
     chromatography
       enzyme linked immunosorbent assay
     diagnostic accuracy
     microscopy
     intermethod comparison
     neutrophil
     human
     male
     female
     major clinical study
     controlled study
    human cell
     adolescent
     aged
    child
```

adult

article
priority journal
Drug Descriptors:
 \*lactoferrin: EC, endogenous compound
 polyclonal antibody
monoclonal antibody
RN (lactoferrin) 55599-62-7

d his

(FILE 'HOME' ENTERED AT 11:41:37 ON 07 JUN 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 11:42:04 ON 07 JUN 2005

	11:42:04 ON 07 JUN 2005
L1	4 S (FECAL LACTOFERRIN) AND POLYCLONAL?
L2	1 DUPLICATE REMOVE L1 (3 DUPLICATES REMOVED)
L3	0 S (TOTAL LACTOFERRIN) AND POLYCLONAL?
L4	0 S LACTOFERRIN? AND POLYCONAL?
L5	19760 S LACTOFERRIN?
L6	279 S (FECAL LEUKOCYTE?)
L7	47 S L5 AND L6
L8	0 S L7 AND POLYCLONAL?
L9	9 S L7 AND ANTIBOD?
L10	4 DUPLICATE REMOVE L9 (5 DUPLICATES REMOVED)
L11	6 S (ENDOGENOUS LACTOFERRIN)

3 DUPLICATE REMOVE L11 (3 DUPLICATES REMOVED)

=>

L12

d his

(FILE 'HOME' ENTERED AT 11:41:37 ON 07 JUN 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 11:42:04 ON 07 JUN 2005

4 S (FECAL LACTOFERRIN) AND POLYCLONAL? L1L2 1 DUPLICATE REMOVE L1 (3 DUPLICATES REMOVED) L3 0 S (TOTAL LACTOFERRIN) AND POLYCLONAL? 0 S LACTOFERRIN? AND POLYCONAL? L4L5 19760 S LACTOFERRIN? 279 S (FECAL LEUKOCYTE?) L6 47 S L5 AND L6 L7 0 S L7 AND POLYCLONAL? L8L9 9 S L7 AND ANTIBOD? L10 4 DUPLICATE REMOVE L9 (5 DUPLICATES REMOVED) L116 S (ENDOGENOUS LACTOFERRIN)

L12 3 DUPLICATE REMOVE L11 (3 DUPLICATES REMOVED)

=>

ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2 ΔN 1992:305244 BIOSIS PREV199294018394; BA94:18394 DN ΤI MEASUREMENT OF FECAL LACTOFERRIN AS A MARKER OF FECAL LEUKOCYTES . GUERRANT R L [Reprint author]; ARAUJO V; SOARES E; KOTLOFF K; LIMA A M; ΑU COOPER W H; LEE A G DIV GEOGRAPHIC MED, DEP MED, UNIV VIRGINIA SCH MED, CHARLOTTESVILLE, VA CS 22908, USA SO Journal of Clinical Microbiology, (1992) Vol. 30, No. 5, pp. 1238-1242. CODEN: JCMIDW. ISSN: 0095-1137. DT Article FS BA LΑ **ENGLISH** ED Entered STN: 27 Jun 1992 Last Updated on STN: 27 Jun 1992 AB While diarrheal illnesses are extremely common in communities and hospitals throughout the world, an etiologic diagnosis may be expensive and cost-ineffective. Although the presence of fecal leukocytes are helpful in the diagnosis and specific therapy of inflammatory diarrheas, this requires prompt microscopic examination of fecal specimens (preferably obtained in a cup rather than a swab or diaper) by a trained observer. We developed a simple, sensitive test for the detection of leukocytes in fecal specimens using antilactoferrin antibody. Whereas radial immunodiffusion detected 0.02 µq of **lactoferrin** (LF) per  $\mu$ l or  $\geq$  2,000 leukocytes per  $\mu$ l, latex agglutination (LA) readily detected ≥ 0.001 µg of LF per  $\mu l$  or  $\geq$  200 leukocytes per  $\mu l$  added to stool specimens. Despite the destruction or loss of morphologic leukocytes on storage for 1 to 7 days at 4° C or placement of specimens on swabs, measurable LF remained stable. Initial studies of stool specimens from six patients with Salmonella or Clostridium difficile enteritis were positive and those from three controls were negative for LF by LA. Of 17 children in Brazil with inflammatory diarrhea (≥ 1 leukocyte per high-power field), 16 (94%) had LF titers of  $\geq$  1:50 by LA, whereas only 3 of 12 fecal specimens with < 1 leukocyte per high-power field on methylene blue examination and none of 7 normal control specimens had an LF titer of > 1:50 by LA. Of 16 fecal specimens from patients with C. difficile diarrhea (cytotoxin titers,  $\geq 1:1,000$ ), 95% (n = 15) had detectable LF by LA (in titers of 1:100 to 1:800). Finally, of 48 fecal specimens from healthy adult U.S. volunteers before and after experimental shigellosis and of 29 fecal specimens from children with documented shigellosis and hospitalized controls in northeastern Brazil, fecal LF titers ranged from 1:200 to  $\geq 1:5,000$  in 96% (25 of 26) samples from patients with shigellosis (and reported positive for fecal leukocytes), while 51 controls consistently had fecal LF titers of We conclude that fecal LF is a useful marker for fecal leukocytes, even when they are morphologically lost on swab specimens or when they are destroyed on transport or storage or by cytotoxic fecal specimens. CCBiochemistry methods - Proteins, peptides and amino acids 10054 Biochemistry methods - Minerals 10059 Biochemistry studies - Proteins, peptides and amino acids 10064 Biochemistry studies - Minerals 10069 Pathology - Diagnostic 12504 Pathology - Inflammation and inflammatory disease Digestive system - Pathology 14006 Blood - General and methods 15001 Blood - Blood cell studies 15004

Blood - Lymphatic tissue and reticuloendothelial system

Pediatrics -

25000 Immunology - General and methods 34502 Immunology - Bacterial, viral and fungal 34504

Medical and clinical microbiology - General and methods 36001

Medical and clinical microbiology - Bacteriology 36002

Medical and clinical microbiology - Serodiagnosis 36504

IT Major Concepts

Blood and Lymphatics (Transport and Circulation); Gastroenterology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Infection; Pathology; Serology (Allied Medical Sciences)

IT Miscellaneous Descriptors

SALMONELLA CLOSTRIDIUM-DIFFICILE ENTERITIS CHILDREN ADULTS SHIGELLOSIS INFLAMMATORY DIARRHEA ANTILACTOFERRIN **ANTIBODY** LATEX AGGLUTINATION IMMUNOLOGIC METHOD DIAGNOSTIC METHOD

ORGN Classifier

Enterobacteriaceae 06702

Super Taxa

Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms

Taxa Notes

Bacteria, Eubacteria, Microorganisms

ORGN Classifier

Endospore-forming Gram-Positives 07810

Super Taxa

Eubacteria; Bacteria; Microorganisms

Taxa Notes

Bacteria, Eubacteria, Microorganisms

ORGN Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

```
ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
    1992:509404 CAPLUS
AN
    117:109404
DN
    Entered STN: 20 Sep 1992
ED
    In vitro test for fecal leukocytes for diagnosis of
TI
    inflammatory diarrhea
    Guerrant, Richard L.; Lee, Amelia G.; Cooper, William H.
IN
    University of Virginia Alumni Patents Foundation, USA
PA
SO
    U.S., 5 pp.
    CODEN: USXXAM
DT
    Patent
    English
LΑ
    ICM G01N033-559
IC
    ICS G01N033-551; G01N033-546
INCL 435007240
    14-7 (Mammalian Pathological Biochemistry)
FAN.CNT 1
    PATENT NO.
                      KIND
                            DATE
                                        APPLICATION NO.
                                        ______
                      ----
                       A 19920623 US 1989-442309 19891128
    US 5124252
PRAI US 1989-442309
                              19891128
CLASS
            CLASS PATENT FAMILY CLASSIFICATION CODES
PATENT NO.
 ______
              ICM
US 5124252
                      G01N033-559
               ICS
                      G01N033-551; G01N033-546
               INCL
                      435007240
                      435/007.240; 435/007.920; 435/007.940; 436/514.000;
              NCL
US 5124252
                      436/534.000
    Inflammatory is distinguished from noninflammatory diarrhea by testing a
AΒ
    fecal sample with an immunoassay for lactoferrin to estimate the number
    of fecal leukocytes. Assays used included a radial
    immunodiffusion assay, a latex agglutination assay, and an ELISA.
ST
    inflammatory diarrhea diagnosis lactoferrin leukocyte
IT
    Lactoferrins
    RL: ANT (Analyte); ANST (Analytical study)
       (determination of, by immunoassay in leukocyte estimation in feces for
inflammatory
       diarrhea diagnosis)
IT
    Leukocyte
       (estimation of, in feces with lactoferrin immunoassay for
       inflammatory diarrhea diagnosis)
IT
    Feces
       (leukocyte estimation in, with lactoferrin immunoassay for
       inflammatory diarrhea diagnosis)
IT
    Antibodies
    RL: BIOL (Biological study)
       (to lactoferrin, for leukocyte estimation in feces for
       inflammatory diarrhea diagnosis)
IT
    Diarrhea
       (inflammatory, diagnosis of, leukocyte estimation in feces with
       lactoferrin immunoassay for)
```

ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1 AN 1996:22064 BIOSIS DΝ PREV199698594199 ΤI Correlation of lactoferrin with neutrophilic inflammation in body fluids. Martins, Clovis A. P.; Fonteles, Maria G.; Barrett, Leah J.; Guerrant, ΑU Richard L. [Reprint author] Box 485, Div. Geographic and Int. Med., Univ. Va. Sch. Med., CS Charlottesville, VA 22908, USA SO Clinical and Diagnostic Laboratory Immunology, (1995) Vol. 2, No. 6, pp. 763-765. ISSN: 1071-412X. DT Article LA English ED Entered STN: 12 Jan 1996 Last Updated on STN: 12 Jan 1996 AB We have reported that lactoferrin, a 77-kDa iron-binding glycoprotein found in secondary neutrophil granules, provides a useful marker of fecal leukocytes in fecal specimens from patients with inflammatory diarrhea (R. L. Guerrant, V. Araujo, E. Soares, K. Kotloff, A. A. M. Lima, W. H. Cooper, and A. G. Lee, J. Clin. Microbiol. 30:1238-1242, 1992). In order to determine the usefulness of this marker of neutrophilic inflammation in different body fluids, we examined blood, gingival swabs, sputum, and saliva using antilactoferrin antibodies (lactoferrin latex agglutination (LFLA)). LFLA titers in whole blood samples were ltoreg 1:4 in all eight samples from patients with neutropenia (absolute neutrophil count (ANC) = lt 150 polymorphonuclear cells (PMNs) per mu-1), ltoreq 1:8 in samples from 13 individuals with moderate leukocyte counts (ANC = 150 to 8,000), and 1:8 to 1:32 in samples from six patients with neutrophilia (ANC gt 8,000). While the overlap precludes a useful role in the identification of neutropenia, these data confirm that lactoferrin titers of gt 1:100 indeed indicate inflammation in fluid specimens. quantitative elution of lactoferrin from gingival swabs, all 7 patients with dental plaque had titers of 1:200 to 1:400; 9 of 12 patients with clinical gingivitis had LFLA titers of 1:200 to 1:1,600, while all 7 individuals with healthy gums and teeth and 4 edentulous patients had LFLA titers of ltoreq 1:100. Eight purulent sputum samples had titers of gtoreg 1:400 (7 were 1:1,600) while 11 normal saliva samples showed titers of ltoreq 1:100. Lactoferrin titers in sputum, gingival swabs, and whole blood correlate with the presence of neutrophils or inflammation in these specimens and may offer a convenient rapid test for inflammatory processes. CC Cytology - Human 02508 Biochemistry methods - Proteins, peptides and amino acids 10054 Biochemistry studies - Proteins, peptides and amino acids 10064 Biophysics - Methods and techniques 10504 Pathology - Diagnostic 12504 Pathology - Inflammation and inflammatory disease Digestive system - Physiology and biochemistry Digestive system - Pathology 14006 Blood - Blood cell studies 15004 15008 Blood - Lymphatic tissue and reticuloendothelial system Immunology - General and methods 34502 Immunology - Immunopathology, tissue immunology 34508 ΙT Major Concepts Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Endocrinology (Human Medicine,

Medical Sciences); Digestive System (Ingestion and Assimilation); Gastroenterology (Human Medicine, Medical Sciences); Immune System

(Chemical Coordination and Homeostasis); Pathology IT Miscellaneous Descriptors

DIAGNOSTIC IMPLICATIONS; **FECAL LEUKOCYTE** MARKER; INFLAMMATORY DIARRHEA; INFLAMMATORY PROCESS; **LACTOFERRIN** LATEX AGGLUTINATION

ORGN Classifier

. . . .

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates